



WDN/SAS 09/07/2001 4239-58378 68645

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*Receipt*

PATENT

Attorney Reference No. 4239-58378

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

(7)

In re Patent Application of: Tosato et al.

Application No. 09/807,148

Filed: April 5, 2001

For: USE OF CALRETICULIN AND CALRETICULIN  
FRAGMENTS TO INHIBIT ENDOTHELIAL CELL  
GROWTH AND ANGIOGENESIS, AND SUPPRESS  
TUMOR GROWTH

Art Unit: 1642

Examiner: To be assigned

Date: September 7, 2001

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper or fee referred to as being attached or enclosed) is being deposited with the United States Postal Service on 9/7/2001 as First Class Mail in an envelope addressed to: Office of Initial Patent Examination Customer Service Center, COMMISSIONER FOR PATENTS, Washington, DC 20231.

*William D. Noonan*

William D. Noonan, M.D.  
Attorney for Applicant(s)

REQUEST FOR CORRECTED OFFICIAL FILING RECEIPT

Office of Initial Patent Examination  
Customer Service Center  
COMMISSIONER FOR PATENTS  
Washington, DC 20231

Sir:

Applicants have received the official Filing Receipt for the application referenced above, a copy of which (with requested correction shown in red ink) is attached as Exhibit A.

The following error(s) appears on the Filing Receipt:

**ERROR**

**Total Claims: 56**

**Total Independent Claims: 11**

**CORRECT INFORMATION**

**Total Claims: 59**

**Total Independent Claims: 12**

Attached is a copy of Response to Notification of Missing Requirements dated May 29, 2001, with attached Exhibits A and B. In that Response, Applicants note that the claims in the present application should be as set forth in the Preliminary Amendment filed April 5, 2001 (Exhibit B thereto).

Applicants request that the identified errors be corrected and that a new official Filing Receipt be issued.

Please return the enclosed postcard to confirm that the items listed above have been received.

Please call the undersigned if any further information is required.

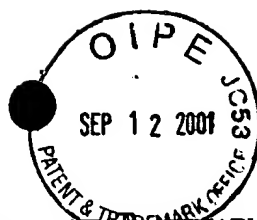
Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By William D. Noonan  
William D. Noonan, M.D.  
Registration No. 30,878

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121 S.W. Salmon Street  
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cc: Docketing



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Page 1 of 4

UNITED STATES PATENT AND TRADEMARK OFFICE

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NIH/SAS/UMD

APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	DRAWINGS	TOT CLAIMS	IND CLAIMS
09/807,148	04/05/2001	1642	2282	4239-58378	27	59	12

CONFIRMATION NO. 2215

24197  
KLARQUIST SPARKMAN CAMPBELL LEIGH &  
WHINSTON, LLP  
121 SW SALMON STREET  
SUITE 1600  
PORTLAND, OR 97204-9446

FILING RECEIPT



\*OC000000006373931\*

Date Mailed: 08/02/2001

Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Customer Service Center. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

Applicant(s)

Giovanna Tosato, Bethesda, MD;  
Sandra E. Pike, North Bethesda, MD;  
Lei Yao, Rockville, MD;

Domestic Priority data as claimed by applicant

THIS APPLICATION IS A 371 OF PCT/US99/23240 10/05/1999  
WHICH CLAIMS BENEFIT OF 60/103,438 10/06/1998

Foreign Applications

Projected Publication Date: N/A

Non-Publication Request: No

Early Publication Request: No

Title

Use of calreticulin and calreticulin fragments to inhibit endothelial cell growth and angiogenesis, and suppress tumor growth

PREVIOUSLY FILED

**Preliminary Class**

424

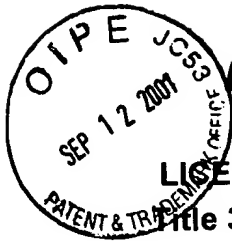
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**Data entry by : NGUYEN, SON**

**Team : OIPE**

**Date: 08/02/2001**





Page 3 of 4  
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**LICENSE FOR FOREIGN FILING UNDER  
Title 35, United States Code, Section 184  
Title 37, Code of Federal Regulations, 5.11 & 5.15**

**GRANTED**

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

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**NOT GRANTED**

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15 (b).

**PLEASE NOTE the following information about the Filing Receipt:**

- The articles such as "a," "an" and "the" are not included as the first words in the title of an application. They are considered to be unnecessary to the understanding of the title.
- The words "new," "improved," "improvements in" or "relating to" are not included as first words in the title of an application because a patent application, by nature, is a new idea or improvement.
- The title may be truncated if it consists of more than 500 characters (letters and spaces combined).
- The docket number allows a maximum of 25 characters.
- If your application was submitted under 37 CFR 1.10, your filing date should be the "date in" found on the Express Mail label. If there is a discrepancy, you should submit a request for a corrected Filing Receipt along with a copy of the Express Mail label showing the "date in."
- The title is recorded in sentence case.

Any corrections that may need to be done to your Filing Receipt should be directed to:

Assistant Commissioner for Patents  
Office of Initial Patent Examination  
Customer Service Center  
Washington, DC 20231



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Tosato et al.

Art Unit: To be assigned

Application No. 09/807,148

Filed: April 5, 2001

For: USE OF CALRETICULIN AND CALRETICULIN  
FRAGMENTS TO INHIBIT ENDOTHELIAL  
CELL GROWTH AND ANGIOGENESIS, AND  
SUPPRESS TUMOR GROWTH

Examiner: To be assigned

Date: May 29, 2001

CERTIFICATE OF MAILING

I hereby certify that this paper and the documents referred to as being attached or enclosed herewith are being deposited with the United States Postal Service on May 29, 2001 as First Class Mail in an envelope addressed to: BOX PCT, COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231.

*William D. Noonan*

William D. Noonan, M.D.  
Attorney for Applicant

BOX PCT  
COMMISSIONER FOR PATENTS  
WASHINGTON, D.C. 20231

**RESPONSE TO NOTIFICATION OF MISSING REQUIREMENTS**

This is a response to the Notification of Missing Requirements for the above-identified U.S. National Stage Application, dated May 8, 2001.

**Claim Fees**

The Notification indicates that the claim amendments made under Article 34 in the parent PCT Application have replaced the claims as originally filed, and accordingly an extra claims fee of \$672 is now due. A copy of the Transmittal Letter that was filed on April 5, 2001 for the instant application is attached as **Exhibit A**. The transmittal letter documents that Article 19 Amendments were not made and will not be made, and notes the submission of a Preliminary Amendment. Applicants respectfully request that the examination of this application refer to the 59 claims as amended in the Preliminary Amendment that was also filed on April 5, 2001 (a copy of which is attached to this Response as **Exhibit B**). Applicants submit, therefore, that the total number of claims is 59, with 12 independent claims and no multiple dependencies.

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Applicants note that a copy of the Article 34 claims was attached to the International Preliminary Examination Report that was filed with the instant application on April 5, 2001. However, this copy of the Article 34 claims was included only as a courtesy to the U.S. Examiner. Do not enter the courtesy copy of the Article 34 claims, or calculate the fee based on these claims. Only enter the Preliminary Amendment dated April 5, 2001, and calculate the fee based on this amendment of the claims as they were before the Article 34 Amendment.

Applicants submit that the total extra claims fee for the 59 pending claims is \$1,422.00, the full amount of which was paid on filing. Applicants submit that no extra claims fee is currently due.

#### Sequence Listing

Also enclosed are a paper copy of the sequence listing for this application, a computer readable copy on diskette, and a statement in compliance with 37 C.F.R. § 1.821 verifying identity of both copies, to comply with the request for the sequence listing pursuant to 37 C.F.R. § 1.821-1.825.

#### Conclusion

If any issues remain before examination of the subject application, the Examiner is respectfully requested to telephone the undersigned Applicants' representative. In particular, if any additional claim fees are required, please telephone the undersigned to discuss this matter.

Respectfully submitted,

KLARQUIST SPARKMAN CAMPBELL  
LEIGH & WHINSTON, LLP


By William D. Noonan  
William D. Noonan, M.D.  
Registration No. 30,878

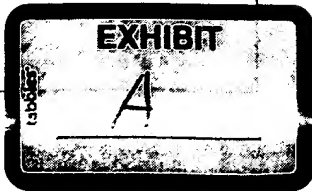
One World Trade Center, Suite 1600  
121 S.W. Salmon Street  
Portland, Oregon 97204  
Telephone: (503) 226-7391  
Facsimile: (503) 228-9446



Date of Deposit: April 5, 2001

FORM PTO-1390 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER 4239-58378
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. § 371		U.S. APPLICATION NO. (If known, see 37 C.F.R. § 1.5)
INTERNATIONAL APPLICATION NO. PCT/US99/23240	INTERNATIONAL FILING DATE October 5, 1999	PRIORITY DATE CLAIMED October 6, 1998
TITLE OF INVENTION USE OF CALRETICULIN AND CALRETICULIN FRAGMENTS TO INHIBIT ENDOTHELIAL CELL GROWTH AND ANGIOGENESIS, AND SUPPRESS TUMOR GROWTH		
APPLICANT(S) FOR DO/EO/US Giovanna Tosato, Sandra E. Pike, and Lei Yao		
<p>Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:</p> <ol style="list-style-type: none"><li><input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. § 371.</li><li><input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. § 371.</li><li><input type="checkbox"/> This express request to begin national examination procedures (35 U.S.C. § 371(f) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. § 371(b) and PCT Articles 22 and 39(1).</li><li><input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19<sup>th</sup> month from the earliest claimed priority date.</li><li><input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. § 371(c)(2))<ol style="list-style-type: none"><li><input type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau).</li><li><input type="checkbox"/> has been transmitted by the International Bureau.</li><li><input checked="" type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</li></ol></li><li><input type="checkbox"/> A translation of the International Application into English (35 U.S.C. § 371(c)(2)).</li><li><input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. § 371(c)(3))<ol style="list-style-type: none"><li><input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau).</li><li><input type="checkbox"/> have been transmitted by the International Bureau.</li><li><input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li><li><input checked="" type="checkbox"/> have not been made and will not be made.</li></ol></li><li><input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. § 371(c)(3)).</li><li><input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. § 371(c)(4)).</li><li><input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. § 371(c)(5)).</li></ol> <p><b>Items 11. to 16. below concern document(s) or information included:</b></p> <ol style="list-style-type: none"><li><input checked="" type="checkbox"/> An Information Disclosure Statement under 37 C.F.R. §§ 1.97 and 1.98.</li><li><input checked="" type="checkbox"/> Letter to the Official Draftsperson.</li><li><input checked="" type="checkbox"/> A <b>FIRST</b> preliminary amendment. <input type="checkbox"/> A <b>SECOND</b> or <b>SUBSEQUENT</b> preliminary amendment.</li><li><input type="checkbox"/> A substitute specification.</li><li><input type="checkbox"/> A change of power of attorney and/or address letter.</li><li><input checked="" type="checkbox"/> Other items or information:<ol style="list-style-type: none"><li><input type="checkbox"/> Written Opinion.</li><li><input checked="" type="checkbox"/> Preliminary Examination Report.</li><li><input checked="" type="checkbox"/> International Search Report.</li><li><input checked="" type="checkbox"/> Copies of References Cited (in Information Disclosure Statement).</li></ol></li></ol>		

  
**24197**





IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Tosato et al.

Art Unit: To be assigned

Application No.: To be assigned

Filed: Herewith

For: USE OF CALRETICULIN AND  
CALRETICULIN FRAGMENTS TO INHIBIT  
ENDOTHELIAL CELL GROWTH AND  
ANGIOGENESIS, AND SUPPRESS TUMOR  
GROWTH

Examiner: To be assigned

Date: April 5, 2001

CERTIFICATE OF EXPRESS MAILING

I hereby certify that this paper and the documents referred to as being attached or enclosed herewith are being deposited with the United States Postal Service on April 5, 2001 as Express Mail Label No. EL754020413US in an envelope addressed to: BOX PCT, COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231.



William D. Noonan, M.D.  
Attorney for Applicant

BOX PCT  
COMMISSIONER FOR PATENTS  
WASHINGTON, D.C. 20231

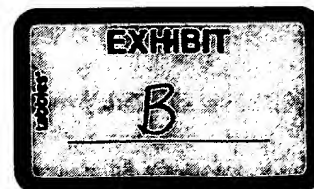
**PRELIMINARY AMENDMENT**

Prior to calculating the fees for the above-identified application, please enter the following amendments:

**In the claims:**

Please add the following claims:

57. (New) The method of claim 1, wherein the therapeutically effective fragment of calreticulin consists essentially of an amino acid sequence selected from the group consisting of:
- (a) the amino acid sequence shown in SEQ ID NO: 5
  - (b) the amino acid sequence shown in SEQ ID NO: 6;
  - (c) the amino acid sequence shown in SEQ ID NO: 8;
  - (d) the amino acid sequence shown in SEQ ID NO: 9; and
  - (e) amino acid sequences comprising fragments and variants of the sequences of (a), (b), (c), and (d), wherein the amino acid sequence inhibits tumor growth.



58. (New) A method of inhibiting radiation induced injury, comprising contacting cells with a pharmaceutical composition comprising at least one protein selected from the group consisting of:

- (a) therapeutically effective fragments of calreticulin;
- (b) therapeutically effective variants of calreticulin; and
- (c) calreticulin.

59. (New) A method of inhibiting chemotherapy induced injury, comprising contacting cells with a pharmaceutical composition comprising at least one protein selected from the group consisting of:

- (a) therapeutically effective fragments of calreticulin;
- (b) therapeutically effective variants of calreticulin; and
- (c) calreticulin.

#### REMARKS

New claims 57-59 have been added. Support for new claim 57 can be found in the specification on page 9, lines 12-13, and on page 3, lines 23-31. Support for new claims 58 and 59 can be found in the specification on page 39, lines 22-24. No new matter has been added. Applicant respectfully requests examination of the application.

#### CONCLUSION

If any issues remain before examination of the subject application, the Examiner is respectfully requested to telephone the undersigned Applicants' representative.

Respectfully submitted,

KLARQUIST SPARKMAN CAMPBELL  
LEIGH & WHINSTON, LLP

By William D. Noonan  
William D. Noonan, M.D.  
Registration No. 30,878

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